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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ADRIAN MERLO, HELMUT MACKE,
JEAN-CLAUDE REUBI, and STEPHAN GOOD

Appeal 2010-012084
Application 10/549,665
Technology Center 1600

Before TONI R. SCHEINER, DONALD E. ADAMS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge.*

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to conjugates with substance P analogues. The Examiner rejected the claims as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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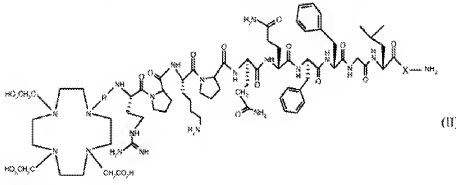
[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

Statement of the Case

The Claims

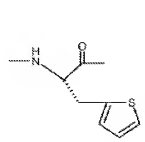
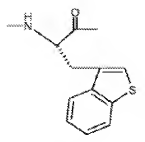
Claims 17-20, 29, and 30 are on appeal. Independent claim 17 is representative and reads as follows:

17. A conjugate of a substance P analogue and a chelator molecule, having the abbreviation Chelator-R-Arg^1-Pro^2-Lys^3-Pro^4-Gln^5-Gln^6-Phe^7-Phe^8-Gly^9-Leu^{10}-X^{11}-NH_2 and the structure of formula I



(II),

wherein
R is -CH_2-C(O)-, -CH(CO_2H)CH_2CH_2-C(O)- or -CH(CO_2H)CH_2-C(O)- and
X is -NH-CH(CH_2CH_2-SO_2-CH_3)-C(O)- (hereinafter abbreviated Met(O_2)^{11}), -NH-CH(CH_2CH_2- SO-CH_3)-C(O)- (hereinafter abbreviated Met(O)^{11}), or -NH-CH[CH(CH_3)CH_2CH_3)-C(O)- (hereinafter abbreviated Ile^{11}), or an analogue of formula II with at least one of the following modifications in the amino acid sequence of substance P analogue:
a) replacement of Leul^{10} by -NH-CH(CH(CH_3)CH_2CH_3)-C(O)- (hereinafter abbreviated Ile^{10}),
b) replacement of Gly^9 by -N(CH_3)-CH_2-C(O)- (hereinafter abbreviated Sar^9),
c) replacement of Phe^7 or Phe^8 or both Phe^7 and Phe^8 by a residue of formula


(2-Thi[7,8]),

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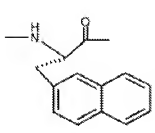
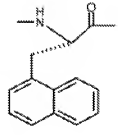
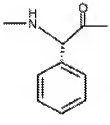
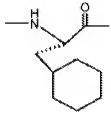
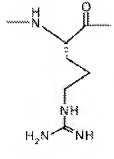
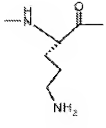

(2-Nal[7,8]),

(1-Nal[7,8]),

(Phegly[7,8]),

(Cha[7,8]),

d) replacement of Lys^3 by residue of formulae


(Arg^3), or

(Orn^3),

e) truncation of 1 to 5 amino acids of the sequence Arg^1-Pro^2-Lys^3-Pro^4-Gln^5, or

f) replacement of 1 to 5 amino acids of the sequence Arg^1-Pro^2-Lys^3-Pro^4-Gln^5 by $N(CH_3)$-CH_2-C(O)- (hereinafter abbreviated Sar),
and wherein the conjugate is unlabelled or labeled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut[h]-212, Bismut[h]-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dyprosium-162, Dysprosium-165, Dysprosium-167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

The issues

A. The Examiner rejected claims 17-20 under 35 U.S.C. § 102(b) as anticipated by Visser[2] (Ans. 4-5).

B. The Examiner rejected claims 17-20 under 35 U.S.C. § 103(a) as obvious over Visser and Coy[3] (Ans. 6-7).

C. The Examiner rejected claims 17-20, 29, and 30 under 35 U.S.C. § 103(a) as obvious over Visser and Li[4] (Ans. 8-10).

A. 35 U.S.C. § 102(b) over Visser

The Examiner finds that "Visser discloses methods for detecting and localizing tissues having neurokinine 1 receptors in the body of a warm-blooded living being by administration of a labeled small peptide having selective affinity to neurokinine 1 receptor, and by then radioassaying" (Ans.

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[2] Visser et al., WO 92/18536 A2, published Oct. 29, 1992.
[3] Coy et al., US 5,750,646, issued May 12, 1998.
[4] Li et al., *DOTA-D-Tyr[1]-Octreotate: A Somatostatin Analogue for Labeling with Metal and Halogen Radionuclides for Cancer Imaging and Therapy*, 13 BIOCONJUGATE CHEMISTRY 721-728 (2002).

4). The Examiner finds that Visser teaches that the "labeled peptide is derived from the following formula (page 4), including substance p and derivatives thereof in examples 1-5" (Ans. 5). The Examiner finds that a "suitable linker for attaching a metal isotope to the small peptide is provided with a chelating group, e.g. DOTA" (Ans. 5).

Appellants contend that it "was surprisingly found that the claimed radio-labelled conjugates are much more effective than DOTATOC, radio-labelled substance P, substance P analogues, saporin, or other small radio-labelled peptides with or without chelating agent in targeting and treatment of tumors, especially brain tumors, e.g., gliomas" (App. Br. 11-12). Appellants contend that "several million different compounds comprise formula (I) [of Visser]. On the other hand, the claimed invention encompasses only one of these millions of compounds . . . which is particularly well suited for the application at issue" (App. Br. 13).

Appellants contend that:

> even if the generic formula (I) of Visser et al. in theory includes the above compound (together with several million others), it fails to particularly teach the species claimed in the present invention. In other words, the claimed species cannot be at once envisioned from the disclosure of Visser et al. as required for a finding of obviousness

(App. Br. 13).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Visser anticipates claim 17?

Findings of Fact

1. Visser teaches that "[s]uitable examples of such a compound of the above general formula I are . . . (2) H-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O_2)-NH_2" (Visser 4, ll. 21-25).

2. Visser teaches that the:

> peptide is labelled with (a) a detectable metal isotope selected from the group consisting of Tc-99m, Pb-203, Ga-67, Ga-68, As-72, In-111, In-113m, Ru-97, Cu- 62, Cu-64, Fe-52, Mn-52m, Cr-51, Na-23, Gd-157, Mn-55, Dy-162, Cr-52 and Fe-56, said metal isotope being attached to said peptide via a suitable linker capable of reacting with an amino group, preferably a terminal amino group, of said peptide, and having a chelating group for chelating said metal isotope

(Visser 2, ll. 23-28).

3. Visser teaches that "[s]uitable linkers are derived from N-containing di- or polyacetic acids or their derivatives, such as . . . 1,4,7,10-tetra-azacyclododecane-N,N',N",N"'-tetraacetic acid (DOTA)" (Visser 6, ll. 5-11).

Principles of Law

The test which determines whether an invention has been anticipated by a reference is whether the description of the invention in the reference is "sufficient to put the public in possession of the invention." *In re LeGrice*, 301 F.2d 929, 933 (1962).

The description of a limited class of compounds by a publication may anticipate compounds within the class, and "it is of no moment that each compound is not specifically named or shown by structural formula in that publication." *In re Petering*, 301 F.2d 676, 682 (CCPA 1962). *See also, In*

re Schauman, 572 F.2d 312, 316-17 (CCPA 1978) (the disclosure of a group comprising a limited number of compounds may provide "a description of those compounds just as surely as if they were identified in the reference by name").

Analysis

Visser teaches a particular analogue of substance P which is identical to the analogue sequence of claim 17 where the modification in b) of claim 17 occurs with the replacement of Gly^9 with Sar^9 and where X^{11} is $Met(O_2)$ (FF 1). Visser expressly teaches that suitable linkers include DOTA (FF 3). We therefore agree with the Examiner that "Visser shows conjugation of sequences which may be considered to be closer prior art than native Substance P, such as example compound 2 on page 4. This compound is directly corresponding with at least modification b) of the instant claims, and can be considered to be closer prior art than the native Substance P sequence" (Ans. 13).

Appellants contend that it "was surprisingly found that the claimed radio-labelled conjugates are much more effective than DOTATOC, radio-labelled substance P, substance P analogues, saporin, or other small radio-labelled peptides with or without chelating agent in targeting and treatment of tumors, especially brain tumors, e,g, gliomas" (App. Br. 11-12).

We are not persuaded. As the Examiner correctly explained, unexpected results do not overcome an anticipation rejection (Ans. 11) (*See In re Malagari*, 499 F.2d 1297, 1303, 182 USPQ 549, 553 (CCPA 1974) ("If the rejection under § 102 is proper, however, appellant cannot overcome it by showing such unexpected results or teaching away in the art, which are

relevant only to an obviousness rejection."). The Examiner also correctly noted that the asserted unexpected results are not commensurate in scope with the instant claims (Ans. 12; *see In re Harris*, 409 F.3d 1339, 1344 (Fed. Cir. 2005) (Unexpected results must also be "commensurate in scope with the degree of protection sought by the claimed subject matter.")). Lastly, the Examiner correctly noted that the comparison was not performed with the closest prior art (*see* Ans. 12-13). "[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991).

Appellants contend that "several million different compounds comprise formula (I) [of Visser]. On the other hand, the claimed invention encompasses only one of these millions of compounds . . . which is particularly well suited for the application at issue" (App. Br. 13).

Appellants contend that:

> even if the generic formula (I) of Visser et al. in theory includes the above compound (together with several million others), it fails to particularly teach the species claimed in the present invention. In other words, the claimed species cannot be at once envisioned from the disclosure of Visser et al. as required for a finding of obviousness

(App. Br. 13).

We are not persuaded. Compound 2 on page 4 of Visser would reasonably lead the ordinary artisan to immediately envisage the species of Claim 17 where the modification in b) of claim 17 occurs with the replacement of Gly^9 with Sar^9 and where X^{11} is $Met(O_2)$ (FF 1-3).

Conclusion of Law

The evidence of record supports the Examiner's conclusion that Visser anticipates claim 17

B. 35 U.S.C. § 103(a) over Visser and Coy

The Examiner finds that with "respect to Applicant's elected species, conjugate DOTA-[Thi^{8},Met(O$_2$)^{11}]- Substance P, Visser does not specifically recite substitution of Thi for Phe at position 8 of the instantly claimed amino acid sequence. Rather, Visser teaches Phe or Tyr at this position (A_6 in the notation of Visser)" (Ans. 6). The Examiner finds that "nonnatural amino acids such as thienylalanine are known in the art to be interchangeable with Phe in similar peptide systems as shown by Coy" (Ans. 6).

The Examiner finds that the "substituted components (Thi and Phe) and their functions were known in the art . . . For example, Coy teaches Phe and Thi to be interchangeable . . . One of ordinary skill in the art could have substituted one known amino acid for another, and the results of the substitution would have been predictable" (Ans. 7).

Appellants contend that it "is noted that Coy fails to remedy the deficiencies of Visser set forth above. Namely, Visser is directed towards millions of compounds and fails to specifically teach or suggest the claimed compounds" (App. Br. 14). Appellants contend that "since Visser et al. fails to teach all the other limitations of the present invention, combining the teachings of these references do not lead a person skilled in the art to the subject matter of claimed invention" (App. Br. 14).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Visser and Coy render claim 17 obvious?

Findings of Fact

4. The Examiner finds that "Coy teaches Phe and Thi to be interchangeable as a given residue in bradykinin antagonist peptides" (Ans. 7).

5. Visser teaches the substance P sequence of "Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH_2" (Visser 4, l. 23).

Principles of Law

A prior art description of a chemical genus often renders a claimed species within the genus prima facie obvious to one of ordinary skill in the art, especially when the claimed composition is used for the identical purpose taught by the prior art. *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989).

Analysis

Visser teaches the sequence of substance P which is identical to the elected sequence of claim 17 where the modification occurs with the replacement of Phe^8 with Thi^8 and where X^{11} is $Met(O_2)$ (FF 5). Visser teaches the use of DOTA as a linker (FF 3). Coy teaches that Phe and Thi were recognized as equivalents (FF 4).

Visser teaches each of the elements and suggests the use of DOTA as a linker and where X^{11} is $Met(O_2)$ (FF 1-3). We agree with the Examiner that it would have been obvious to substitute known equivalent amino acids such as Thi for Phe where they have been shown to function in analogous

systems (FF 4). *See In re Susi*, 440 F.2d 442, 445, 169 USPQ 423, 425, 58 CCPA 1074 (1971) (obviousness rejection affirmed where the disclosure of the prior art was "huge, but it undeniably include[d] at least some of the compounds recited in appellant's generic claims and it is of a class of chemicals to be used for the same purpose as appellant's additives").

Conclusion of Law

The evidence of record supports the Examiner's conclusion that Visser and Coy render claim 17 obvious.

C. 35 U.S.C. § 103(a) over Visser and Li

Appellants do not separately argue the claims in this obviousness rejection. Having affirmed the rejection of Claim 17 over Visser, we also find the further combination with Li renders the claims obvious for the reasons given by the Examiner (Ans. 8-10).

SUMMARY

In summary, we affirm the rejection of claim 17 under 35 U.S.C. § 102(b) as anticipated by Visser. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 18-20, as these claims were not argued separately.

We affirm the rejection of claim 17 under 35 U.S.C. § 103(a) as obvious over Visser and Coy. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 18-20, as these claims were not argued separately.

We affirm the rejection of claim 17 under 35 U.S.C. § 103(a) as obvious over Visser and Li. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006),

we also affirm the rejection of claims 18-20, 29, and 30, as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1).

AFFIRMED

dm

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